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# EFFECT OF FLYING ON FIBRINOLYTIC ACTIVITY IN THE BLOOD OF JET PILOTS

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# EFFECT OF FLYING ON FIBRINOLYTIC ACTIVITY IN THE BLOOD OF JET PILOTS

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E. Kuhnke*

By fibrinolysis we mean the destruction of a fibrin clot which has been formed. Fig. 1 shows a schematic representation of the relationships involved: When there is bleeding, the fibrin clot develops from the monomolecular fibrinogen, under the influence of thrombin. The reticulum, which is loose to begin with, is made to retract by the blood platelets. This retracted clot seals the bleeding vessel watertight. Under normal conditions, the clot remains until it is replaced by connective tissue. However, if fibrinolysin operates on the clot, the fibrin is depolymerized: The clot dissolves, and bleeding begins again. When fibrinolytic activity is very high, no solid clot is formed at all.

The intensity of fibrinolytic activity can be either inhibited or stimulated (Fig. 2). Under normal conditions, it is just high enough to counterbalance the latent clotting. If a condition of ergotropic reaction predominates, the stimulating factors win the upper hand, and fibrinolytic activity is intensified. This is how emotional stresses and physical strains have their effect. Drugs can also influence the equilibrium.

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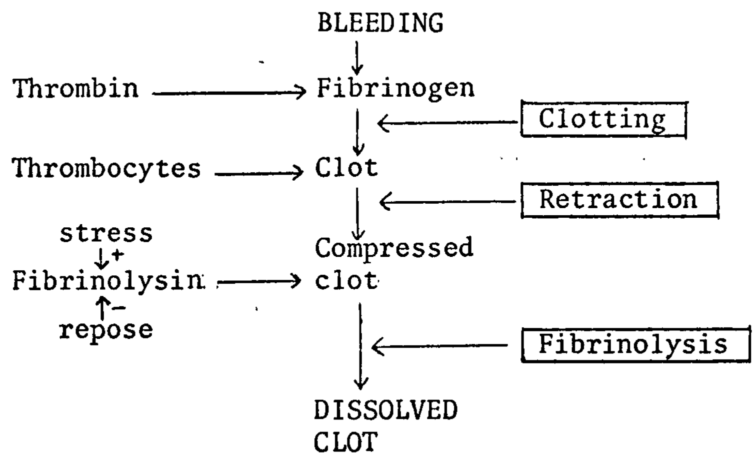



Fig. 1. Schematic representation of clotting, retraction, and fibrinolysis.

Streptokinase triggers intense fibrinolytic activity, and ε-aminocaproic acid can completely inhibit it.

Thus, if fibrinolytic activity is known, one method of investigation yields two pieces of information which are equally important:

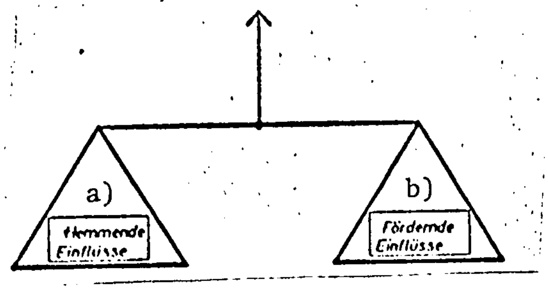
1. Since increasing physical and emotional stress brings about increased activity in the fibrinolytic potential, if we know the repose value we can draw conclusions about the severity of the stress.
2. Increased activity on the part of the fibrinolytic potential also signifies, however, a disturbance of clot formation and the danger of premature destruction of blood clots.

If we want to concentrate here on the relationship between the extent of the increase in fibrinolysis and the severity of the stress, however, we should consider the no less important possibility of a disturbance in hemostasia.

The findings discussed here refer immediately to the group which we studied, that is, Starfighter pilots. However, these findings are also valid

Fibrinolytic Activity

none weak medium intense extremely intense




a = inhibiting influences

b = stimulating influences

REPOSE | latent fibrinolysis | EXCITATION
Sleep | | Emotional stress
 | | Physical exertion
ε-aminocaproic acid | | Streptokinase

Fig. 2. Fibrinolysin as an agent of equilibrium.

for other conditions which place high demands on the organism, such as long and tiring automobile trips, the emotional stress of patients facing surgery, and women in labor. Studying pilots offers a variety of favorable prerequisites:

1. In terms of age, the group is relatively homogeneous. With a few exceptions, the pilots we studied were all between 25 and 35 years old.
2. All subjects were under medical supervision. Thus, we could safely assume that our test personnel were physically and emotionally in perfect health.
3. Living conditions are largely similar for all group members.

It was not possible to obtain rest-and-fasting values.

Consequently, we refer our stress values to the starting value. This is the value which was generally found shortly before the first flight of the day on which we were studying the pilots. The results come from the following:

1. From the retraining period. In the weapons school, jet pilots who have flown other aircraft previously are retrained for the F-104 type. In the process, the whole flight program is practiced. On the average, flight time was 50 minutes.
2. From bombing exercises. These pilots came from combat squadrons and had been trained there. Flying time was 50 minutes, 4 times a day. During each flight, four approach flights were carried out at low altitudes, with subsequent bomb-dropping during the steep climbing phase. The average figure for the total daily flying time is 200 minutes.
3. From low-level flight navigation exercises in a combat squadron. The maximum daily flight time was 2 hours, 3 times a day, i.e. 360 minutes.

We can classify the stresses to which the pilots were exposed into physical and emotional ones.

The physical stresses involve primarily forces of acceleration (Fig. 3). We classify them according to the direction in which they act: Transversal (chest-back direction), positive (head-foot direction), and negative (foot-head direction) forces.

If we ignore certain flight exercises during retraining, the pilots were briefly exposed to forces acting in the positive direction only during bombing exercises. Generally, the physical stress consisted of transversal

Forces of Acceleration

(Boundary values)

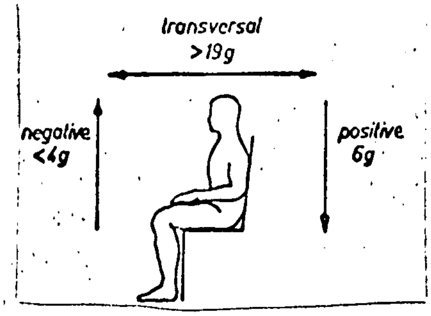



Fig. 3. Tolerated accelerations during flight as a function of the direction of action.

acceleration forces of less than 2 g during takeoff and landing. Since more than 19 g can be tolerated in this direction, it is clear that no noteworthy stresses occur during these flight phases. The same holds true for the fighter-bomber pilots we studied during flight.

The emotional stresses during flight are definitely in the fore. Very intensive concentration during the whole flight is demanded of the pilot of such a fast aircraft. Moreover, attention must be divided among several simultaneous processes. The pilot must be always ready to react quickly and accurately to unexpected situations. Observation and action, automatic control motions and voluntary reactions must be perfectly coordinated. It is easy to understand how personal and official worries can significantly affect a pilot's output (Eberling [1]).

According to statements by Starfighter pilots, the greatest stresses occur when they are flying at low altitude in critical weather or at night, so that they must perform the tasks which are otherwise divided among the pilot, copilot, navigator, radio operator, and flight engineer, simultaneously and with maximum precision.

Since signs of exhaustion, together with a letup in concentration and coordination, are primarily phenomena of the central nervous system, the pilot's internal attitude to flying and to the particular type of aircraft plays an important role. We should also add that all pilots are enthusiastic aircraft commanders. They do not face the F-104 with the reluctance we might expect. However, they would prefer a twin-jet aircraft with a two-man crew to the Starfighter, due to the reduced emotional stress.

## METHOD

The greatly simplified schematic digram of the method of study (Fig. 4) shows that the blood acquired from venous puncture was made incoagulable with sodium citrate. Then it was centrifuged until the cells precipitated out, and the remaining plasma was put in acetic acid. The precipitated euglobulins and enzymes were centrifuged later, and the sediment was dissolved in a borate solution. (A detailed description of the method is given in Kuhnke et.al. [2] and Kuhnke [3].) In a cuvette, the colloidal solution was made to clot, by adding calcium chloride. During the coagulation, the turbidity of the deposit increases. This increase in extinction is measured photometrically. After some time, the clot begins to dissolve once more. This can be seen from the decrease in extinction in the photometer. The time passing between the start of clot formation and the end of fibrinolysis has been designated as the fibrinolysis time $t_1$.

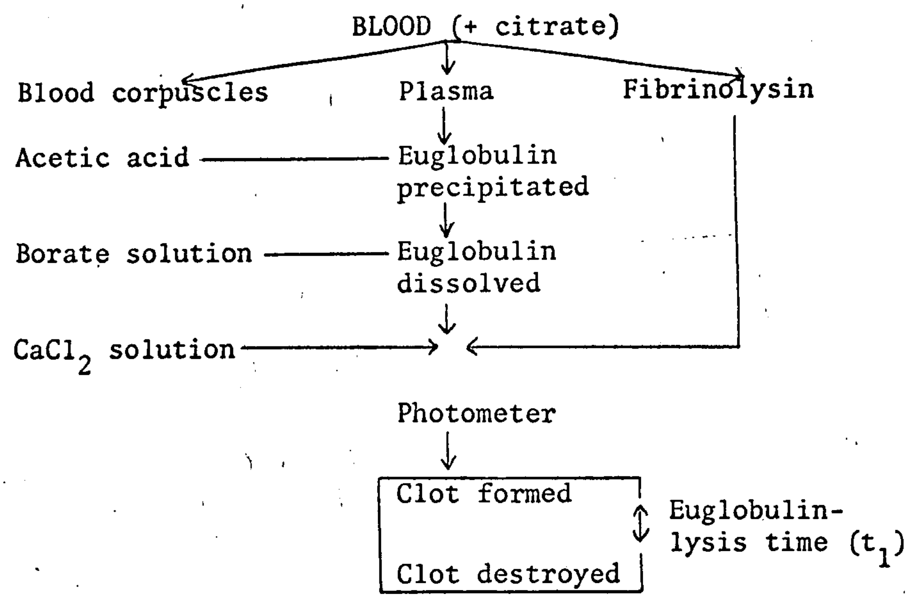



Fig. 4. Simplified schematic diagram of method used to measure euglobulin-lysis time.

Fig. 5 is a schematic diagram of the photometric record. In the lysogram, the ordinate shows the extinction, and the abscissa, the time. Lysis time $t_1$ begins when the curve bends away from the horizontal. This is the time point at which fibril formation begins. When coagulation has ended, the curve is again parallel to the time axis. The increase in extinction caused by the clotting is designated $\Delta E$. After some time, the extinction begins to diminish, independently of the fibrinolytic activity. Finally, it reaches the initial value once more. This is also the time at which lysis ends.

There is a relationship between the fibrinolysis time and fibrinolytic activity: The logarithms of $t_1$ and of activity are inversely proportional. Accordingly, a short lysis time corresponds to high activity, and vice versa.

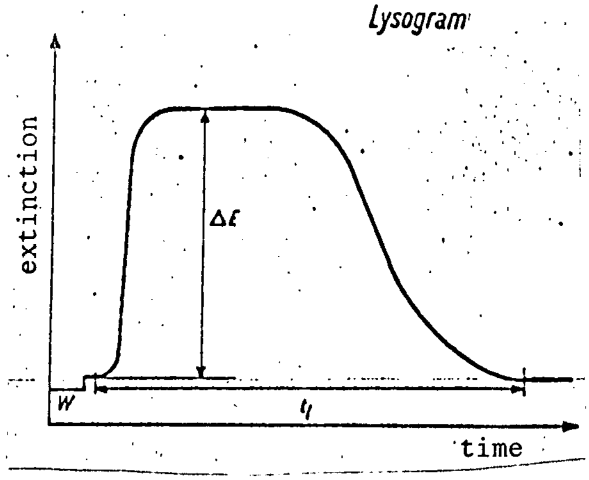



Fig. 5. Schematic diagram of a lysogram. $t_1$ = lysis time; ΔE = change in extinction in the deposit, caused by clot formation.

## FINDINGS

The results presented here are based only on flights which went normally. All flight emergencies -- that is, situations which acutely threatened life -- were left out of consideration

During retraining (Fig. 6), an average initial value of 192.3 minutes was found for the euglobulin-lysis time. If we equate this value with 100%, there is an average drop of 44% -- to 56% -- for the whole flight program. This signifies an important intensification of fibrinolytic activity, for the clot's durability has been cut almost in half. The individual flight hours are varying critical. Below, we will return to the differences which result from this.

Thus, a combat pilot who is already retrained and has experienced daily flights does not generally exhibit this much shortening of the fibrinolysis time after flying for 50 minutes (Fig. 7). In one of these pilots, we found a decrease by only 4%, to 96%, after 50 minutes of flight during bomb-dropping exercises. After the second flight, i.e. after 100 minutes of flight time,

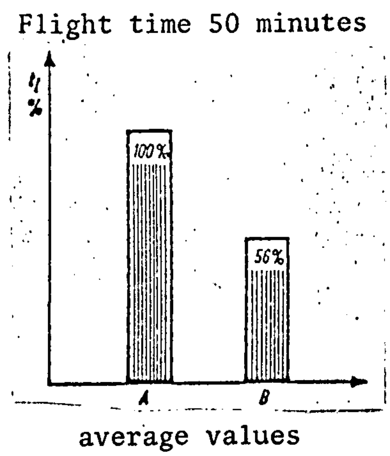



Fig. 6. Shortening of lysis time during retraining for the F-104. Average values for the whole flight program.

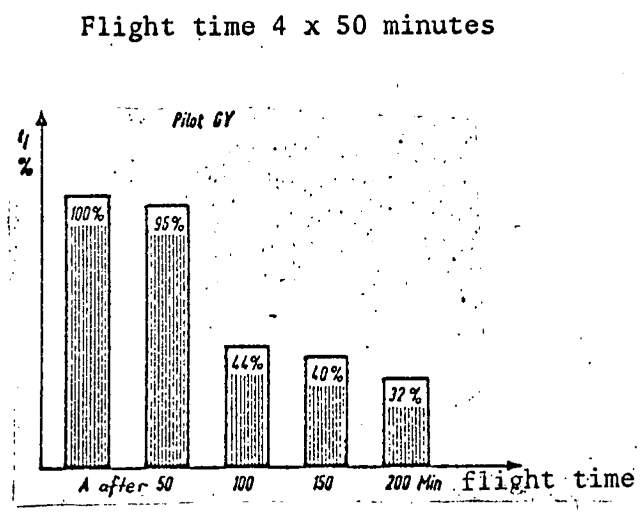
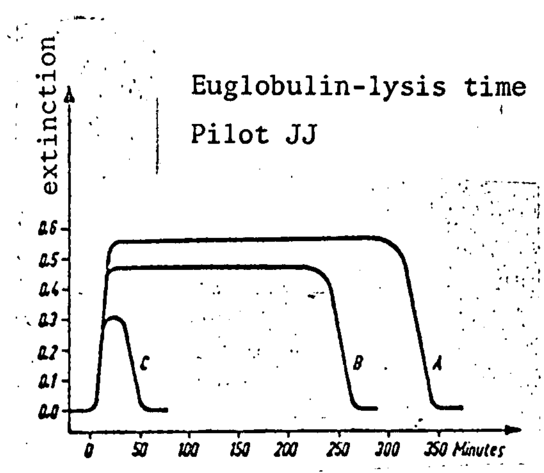



Fig. 7. Shortening of lysis time with 4 x 50 minutes of flight time (bombing exercises).

$t_1$ has already dropped to 44%, however; after the third flight, to 40%; and after the fourth flight, all the way to 32% of the initial value. Thus, the durability of the clot is only one third of the initial value.

Fig. 8 is a schematic representation of the lysograms for another pilot. The initial lysogram, designated by A, exhibits a high rate of increase of extinction during clotting and then a clear plateau, which proves the existence of a stable clot. After 2 hours of low-level flight navigation, both $t_1$ and $\Delta E$ have dropped. However, a plateau still exists. After another 2 hours of flight, $t_1$ is very short, and the increase in extinction is even smaller. There is no plateau at all. The rising branch of the lysogram arches over to the falling branch. This curve shape indicates that fibril formation and fibril destruction merge continuously into each other. Most likely, fibrinolysis is very intense even as the first fibrin fibrils are developing.




A = before flight
B = after 2 hours flight
C = after 4 hours flight

Fig. 8. Changes in the lysogram after low-level flight navigation exercises. Schematic representation based on measured values.

| Pilot JJ | $t_l$ | $\Delta E$ |
|---|---|---|
| Initial value | 350 Min. = 100% | 0,56 = 100% |
| Flight time 2 hours | 271 Min. = 77% | 0,47 = 83% |
| Flight time 4 hours | 57 Min. = 16% | 0,31 = 55% |

Fig. 9. Tabular compilation of measured values (cf. Fig. 8).

The table (Fig. 9) compiles the measured values for this pilot. The lysis time dropped from 100% before the first flight to 77% after 2 hours of flying and 16% after 4 hours. Thus, the durability of the clot dropped to about one sixth. Here, $\Delta E$ also drops from the initial value (= 100%) to 83% after 2 hours of flight and 55% after 4 hours. This means that at the curve's apex -- that is, at the time of maximum clot size -- the optical density of the clot is only about half of the repose value for optical density.

Fig. 10 shows the results for another pilot after low-level flight navigation. The initial value of $t_1$ = 100% has dropped to 44% after 2 hours. After 4 hours of flight time, no clot is even formed at all. The fibrin fibrils are also destroyed in rapid succession, as quickly as they are formed. It is also possible that no fibrils are even formed from the fibrin monomers which come from the fibrinogen, because even the monomers are destroyed by the high fibrinolytic activity.

At this point, it must be mentioned that our method improved the sensitivity of demonstrating fibrinolytic activity. It is not permissible to conclude, therefore, that no more coagulation would take place at all in these pilots in vivo. However, from other observations -- such as, for example, the behavior of the clot with the retraction sediments -- we can conclude that

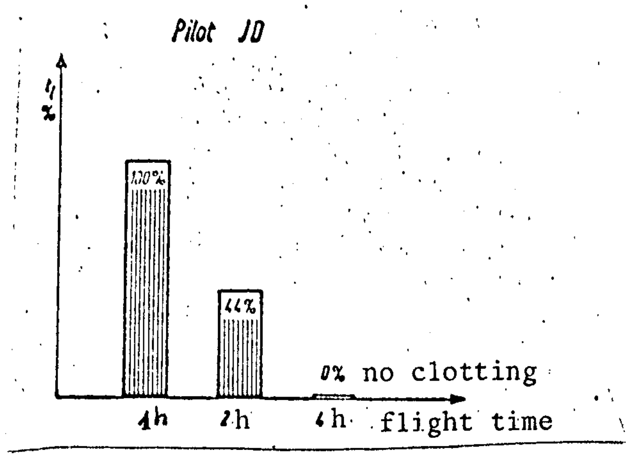
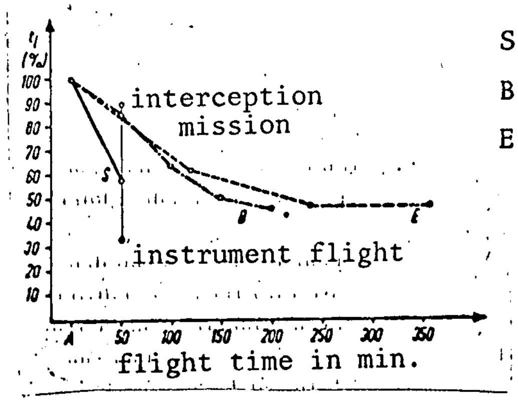



Fig. 10. Value of $t_1$ before low-level flight navigation and after 2 and 4 hours of flight.

this condition has already been approached very closely. Consequently, danger can result to wounded pilots if during infusions they are given only blood-substitute fluids, instead of blood or plasma. A more precise investigation of this effect has not yet been made.

Fig. 11 gives a summary view of results during retraining, bombing exercises, and low-level flight navigation exercises. In each case, the initial values are designated as 100%. The sharp decrease in the lysis time during training (Curve S) after a flight time of only 50 minutes is quite conspicuous. I mentioned above the varying criticality of the individual flight hours. The interception-flight exercise ($t_1$ = 89%) and the instrument-flight hour ($t_1$ = 34%) were drawn in this diagram to demonstrate extreme values. Here, the proportion which physical and emotional stresses have in the overall stress can be clearly seen: During the interception mission, which is relatively active from a fibrinolytic point of view, the pilot is exposed to intensive forces of acceleration during flight. The instrument-flight exercises, Lysis time as a function of flight time and flight mission

(average values)




S = training

B = bombing exercises

E = combat-flight exercises

Fig. 11. Changes in $t_1$ (average values) during retraining, bombing exercises, and low-level flight navigation exercises.

on the other hand, which demand high concentration but involve practically no acceleration forces, significantly intensify fibrinolytic activity.

The type of flight mission seems to have little or no effect on the shortening of $t_1$ in experienced combat pilots, as a comparison of Curves B and E shows. Rather, it seems that flight time plays the decisive role. Nothing definite can be said about this important question, since the number of studies is still too small.

In some of the studies, we took blood from the pilots as early as 2 or 3 minutes after landing. In general, however, it was 20 to 40 minutes after landing before they were in the examination room.

In order to see how fibrinolytic activity changes with time after a stress is over, we carried out supplementary studies. For this purpose, we selected a 4000-meter cross-country race, which was set up in such a way that the subjects exhausted their full reserves of energy. Blood was

Lysis time and physical stress

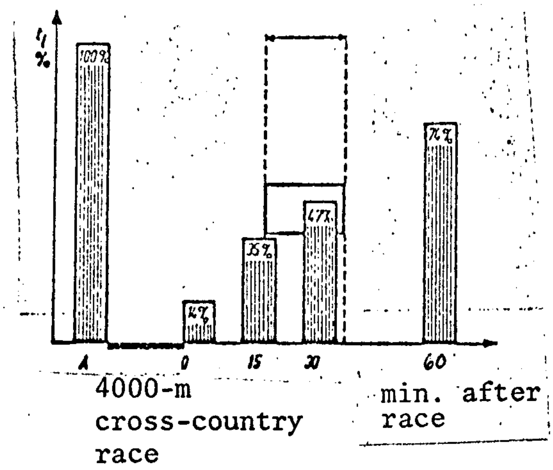



Fig. 12. Euglobulin-lysis time after physical stress (4000-meter cross-country race) is over, as a function of the time at which blood is taken (average values); see text.

taken from our test personnel right before the race, and then immediately after the race, as well as 15, 30, and 60 minutes later.

Fig. 12 shows the average values from eight cross-country races. Immediately after the race, $t_1$ has dropped from its initial value of 100% to 14%. After that, fibrinolytic activity drops very rapidly, since $t_1$ rises relatively quickly, reaching 35% of the initial value after only 15 minutes, 47% after 30 minutes, and 74% after 60 minutes.

If we now consider the time span between 20 and 40 minutes, during which the pilots came to us, and the rise in average values with time, a rectangle results (see Fig. 12).

Accordingly, for the cross-country race, within the period from 20 to 40 minutes, we can expect a shortening of $t_1$ to 38.5% as a maximum average value and to 55% as a minimum. If we use these figures as a basis for activation caused by flying, we see that the maximum value is reached after 50 minutes for retraining, after 130 minutes for bombing exercises, and after about 160 minutes for combat-flight exercises. In this way, we can draft a relatively reliable picture of the stresses which Starfighter pilots are exposed to during daily flight programs.

It is also found that only a few pilots exhibit an initial value for fibrinolysis time which equals the normal value for nonflying personnel. On the average, even the morning value exhibits higher activity. In addition, there is the daily activation of the fibrinolytic potential, which ranges from intense to very intense.

At present, we can only make statements about the short-term effects of flying. To determine whether and how constant significant stresses affect the body after years of flying must await further investigation.

On the basis of these findings, the following recommendations are made, within the framework of medical precautions:

1. A supplementary vacation under official supervision -- if possible, in the middle between two vacation periods -- will probably greatly promote restitution of the organism.
2. For the case of flight accidents, all air bases should provide, in addition to blood supplies, fibrinolysis inhibitors as well, for example, ε-aminocaproic acid. It is precisely in the first hours after being injured that this kind of treatment is particularly necessary, as well as effective.
3. Until tolerated blood dilutions have been examined, only blood or plasma should be used for infusions to wounded pilots, but no blood substitutes.

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[illegible]nvestigation of the relationship between the extent of the [illegible] of fibrinolysis and the degree of stress to which human [illegible]nism is subjected. By using a special test method, a group of test [illegible] was tested during normal flights aboard the Starfighter aircraft. The results obtained in these measurements are presented and discussed. They also apply to other high-stress states in human organism. O.H.